IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

WILSON WOLF MANUFACTURING CORPORATION, Plaintiff, vs. BRAMMER BIO, LLC, Defendant.	Case No.: _____ **JURY TRIAL DEMANDED**

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Wilson Wolf Manufacturing Corporation ("Wilson Wolf"), for its Complaint against Defendant Brammer Bio, LLC ("Brammer Bio"), states and alleges as follows:

THE PARTIES

1. Plaintiff Wilson Wolf is a corporation organized under the laws of the State of Minnesota, with its principal place of business in New Brighton, Minnesota.

2. Upon information and belief, Defendant Brammer Bio is a limited liability company organized under the laws of the state of Delaware with its registered agent located at 1675 South State Street, Suite B, Dover Delaware.

JURISDICTION AND VENUE

3. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a), as this is an action for patent infringement arising under the patent laws of the United States, 35 U.S.C. § 1 *et seq.*

4. This Court has personal jurisdiction over Brammer Bio because it is a Delaware corporation and essentially "at home" in this District. Further, Brammer Bio has caused tortious injury to Wilson Wolf through its acts of patent infringement, and on information and belief, regularly does or solicits business, or engages in a persistent course of conduct in this District or derives substantial revenue from things used or consumed in this District.

5. Venue is proper in this District under 28 U.S.C. §§ 1391(b)(1) and 1400(b), because Brammer Bio is incorporated under the laws of Delaware and has its designated registered agent located in this District, and therefore "resides" in this District within the meaning of those statutes.

FACTUAL ALLEGATIONS

I. Wilson Wolf Develops Innovative Devices and Methods to Grow Cells

6. Wilson Wolf is a leader in the design of innovative devices and methods to grow cells in a laboratory environment.

7. The process of growing cells in a laboratory environment is called "culturing" cells. Innovative cell culture technology allows a lab to grow cells in greater volume, to grow cells faster, and to grow cells with lower risks of contamination.

8. Cell culture technology is critical to many fields, including biology and medicine. Cell culture technology is important, for example, when cells are grown for purposes of scientific investigation and research. Scientists grow cells to study how cancer develops and evolves. In contrast, doctors grow cells to diagnose cancer in a particular patient, and to select and calibrate treatment options for that patient. Cell culture technology is also used when cells are grown for commercial production of medications. For example, drug companies grow cells that produce monoclonal antibodies and other proteins that are used to treat diseases. These medications produced by cells are sometimes referred to as "biopharmaceuticals."

9. Cells in culture can also be used to replicate specially engineered "viral vectors" in large quantities. These viral vectors can be introduced into a patient to treat genetic disorders. This is known as "gene therapy."

10. Another rapidly-expanding field of cell culture technology involves the production of cells which can *themselves* be used to treat diseases. Some cells naturally occurring as part of the body's immune system are very good at fighting illnesses. For example, certain lymphocytes naturally infiltrate tumors and attack cancerous cells, while "natural killer" cells help the body fight viral infections. Unfortunately, the patient's body typically does not have enough of these cells to mount an effective immune system response to overcome the illness. Using cell culture techniques, a small quantity of these cells from the patient can be expanded into an "army" of cells that can be reintroduced to the patient to support recovery.

11. Wilson Wolf has developed devices and methods that have revolutionized the process of culturing cells.

12. In order to grow, cells need food and oxygen. To provide food, cells are typically grown in a liquid medium that contains nutrients for the cells. To provide oxygen, many devices rely on the oxygen in the gas residing above the liquid medium. Oxygen enters the liquid medium through the gas-liquid interface and is available to the cells.

13. Prior to Wilson Wolf's innovations, the conventional wisdom was that nutrients do not move very far in the liquid medium. As a result, cells only benefit from liquid medium very close to them; excess medium is wasted, and medium is very expensive. Based on that conventional wisdom, cells were typically being grown in flasks with a very thin (2-3 mm) layer of liquid medium; the vast majority of the flask contained no medium and no cells, wasting a significant amount of space. Also according to conventional wisdom, oxygen could only travel a

short way into the liquid medium. If a flask contained more than a very thin layer of liquid medium, the medium would suffocate the cells.

14. The traditionally shallow depth of liquid medium led to inefficient use of space. For example, one manufacturer recommends a working volume of 0.2 mL to 0.3 mL per square centimeter of cell growth surface area in the cell culture flask. For a standard 225 cm^2 flask with 850 mL of total volume, the recommended working volume is 45 mL to 67.5 mL. With a recommended working volume of 45 mL to 67.5 mL, only a small fraction of the space that the flask occupies is being used to grow cells. The remaining space is just gas. This wasted space above the thin layer of liquid medium is often referred to as "head space."

15. The image below illustrates the traditional shallow depth of medium in a cell culture flask. The liquid medium is the thin red/orange layer in the bottom of the flask. The flask is mostly empty. The empty space above the thin layer of liquid medium is the headspace.

16. The traditional limits on the amount of liquid medium per flask meant that one had to culture cells in multiple flasks in order to obtain a given volume of culture. For example, to obtain a 1000 mL volume of culture, one would need to culture cells in 15 to 22 T-225 cm^2 flasks with a working volume of 45 mL to 67.5 mL each. The requirement that 15 to 22 devices be fed and monitored increases labor costs and contamination risks.

17. The inefficient use of space in a cell culture flask is compounded by the fact that cells are typically cultured in an incubator. The incubator provides a controlled temperature and gas environment. Incubator space is limited. And only so many flasks can fit within a given volume of incubator space. Inefficient use of flask space therefore leads to inefficient use of incubator space. Based on conventional wisdom about medium thickness, decades of cell culture devices and methods made inefficient used of flask and incubator space. As a result, the process of culturing cells was slower, more cumbersome, and more prone to contamination than necessary.

18. Wilson Wolf challenged the conventional wisdom and developed devices and methods that grew more cells, in less space, with less labor and lower risk of contamination. Wilson Wolf challenged the conventional wisdom in at least two related ways. First, instead of

having cells "breath" through a thin layer of liquid medium, Wilson Wolf had cells "breath" through a gas permeable membrane. With gas permeable material, instead of relying on the headspace within the device as a source of oxygen, cells can get oxygen from outside the device. This eliminated the need for headspace within the device. Second, Wilson Wolf found that nutrients and oxygen could move further in the medium than the conventional wisdom taught. This eliminated the design constraint imposed by the conventional wisdom that the liquid medium should be confined to a thin layer above the cells.

19. By using these insights, Wilson Wolf pioneered several new device designs and cell culture methods. In one design, a device with a single gas-permeable growth surface could support far more medium than taught by the conventional wisdom, allowing cell growth to proceed for a longer time before replenishing the medium. In another design, multiple growth surfaces could be stacked in a single device filled with medium, increasing the number of cells grown in a given volume of space. Other designs combined multiple growth surfaces with more medium than taught by the conventional wisdom. Wilson Wolf has been awarded several U.S. patents for its innovative cell culture devices and methods, including the patents in suit.

II. Wilson Wolf's Asserted Patents

20. Wilson Wolf owns U.S. Patent No. 9,441,192 ("the '192 Patent"), entitled "Cell culture methods and devices utilizing gas permeable materials," which issued on September 13, 2016. A copy of the '192 Patent is attached as Exhibit A.

21. Independent claim 1 of the '192 Patent is set forth below:

> 1. A method of culturing cells comprising:
>
> adding medium and animal cells into a static cell culture device that is not compartmentalized by a semi-permeable membrane, at least a portion of said cell culture device is comprised at least in part of a non porous gas permeable material, ambient gas is in contact with at least a portion of said gas permeable material, and
>
> placing said cell culture device in a cell culture location that includes ambient gas at a composition suitable for animal cell culture, wherein said cell culture device is oriented in a position such that at least a portion of said cells reside upon at least a portion of said gas permeable material, the uppermost location of said medium is elevated beyond 2.0 cm from the lowermost location of said medium, and said device is in a state of static cell culture.

22. Wilson Wolf owns U.S. Patent No. 9,732,317 ("the '317 Patent"), entitled "Highly efficient gas permeable devices and methods for culturing cells," which issued on August 15, 2017. A copy of the '317 Patent is attached as Exhibit B.

23. Independent claim 6 of the '317 Patent is set forth below:

> 6. A static cell growth apparatus comprising:
>
> a liquid impermeable housing, the inside of which is able to contain cells and medium and the outside of which is in contact with ambient gas; and
>
> the housing defining a plurality of gas permeable shelves, each having an inside surface and an outside surface; and
>
> the inside surface of each shelf having an opposing surface located a distance away and defining a culture space; and
>
> the culture spaces are located one above the other when the shelves are in a horizontal position; and

a manifold that connects the culture spaces; and

projections that make contact with the outside surface of each shelf while leaving a portion of the outside surface in contact with ambient gas.

24. Wilson Wolf owns U.S. Patent No. 8,697,443 ("the '443 Patent"), entitled "Cell culture methods and devices utilizing gas permeable materials," which issued April 15, 2014. A copy of the '443 Patent is attached hereto as Exhibit C.

25. Independent claim 26 of the '443 Patent is set forth below.

26. A method of culturing cells in a cell culture device comprised at least in part of a gas permeable material and including at least one access port and including at least two scaffolds, the method comprising:

a) adding cells and a volume of liquid medium into said cell culture device;

b) orienting said cell culture device into an inoculation position such that said scaffolds reside at different elevations within said cell culture device;

c) allowing cells to settle upon said scaffolds;

d) adding enough liquid medium to prevent a unique gas-liquid interface from forming directly above at least one scaffold when the device is oriented in the inoculation position and to have at least a portion of the liquid medium in contact with at least a portion of said gas permeable material;

e) placing the cell culture device in a cell culture location that includes ambient gas at a composition suitable for cell culture, said ambient gas making contact with said gas permeable material; and

f) not perfusing said liquid medium when said device is in said cell culture location.

III. Brammer Bio Infringes Wilson Wolf's Patents

26. Brammer Bio is a contract development and manufacturing organization (CDMO) that develops cell culture processes and grows cells and viral vectors on a contract basis for others. Brammer Bio's website states that the company's vision is "To be the best-in-class gene therapy CDMO." See Exhibit D (website excerpts) (https://www.brammerbio.com/our-team). Brammer Bio's website also states: "We have supplied more than 150 lots for our clients, many for first-in-

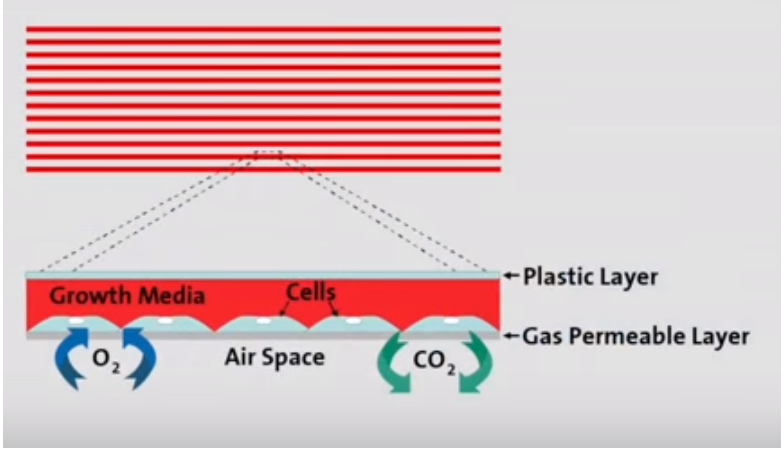
human trials. We develop customized solutions for clients' breakthrough therapeutics and are ready to support clients through licensure and commercial supply." Id. (https://www.brammerbio.com/our-team). Brammer Bio's website further states that its development and manufacturing capabilities extend to the "Full-range of production platforms including ***flat stock***, 50L - 2000L stir tank, perfusion, etc." Id. (https://www.brammerbio.com/gene-therapy-manufacturing) (emphasis added). A July 2018 presentation by Brammer Bio's Chief Manufacturing Officer, Christopher Murphy, entitled "Upstream Manufacturing Platform for Gene Therapy Viral Vectors," lists the HYPERStack as "flat stock" used as an upstream manufacturing platform for anchorage dependent cells. See Exhibit E, at 9. An article co-authored by Brammer Bio's President and CEO, Mark Bamforth, and its Chief Scientific Officer, Richard Snyder, entitled "Investing for Successful Advancement of Viral Vector Manufacturing," states that CDMOs, like Brammer Bio, must offer a wide range of cell growth platforms, including platforms like the HYPERStack. See Exhibit F at 2. On the LinkedIn professional networking site, Brammer Bio staff have documented their use of the HYPERStack to grow cells at Brammer Bio.

27. Brammer Bio has infringed the patents in suit through its use of the Corning HYPERStack cell culture device. The HYPERStack is a multiple-shelf device that uses gas-permeable material to oxygenate cells. In use, the device is filled with liquid medium.

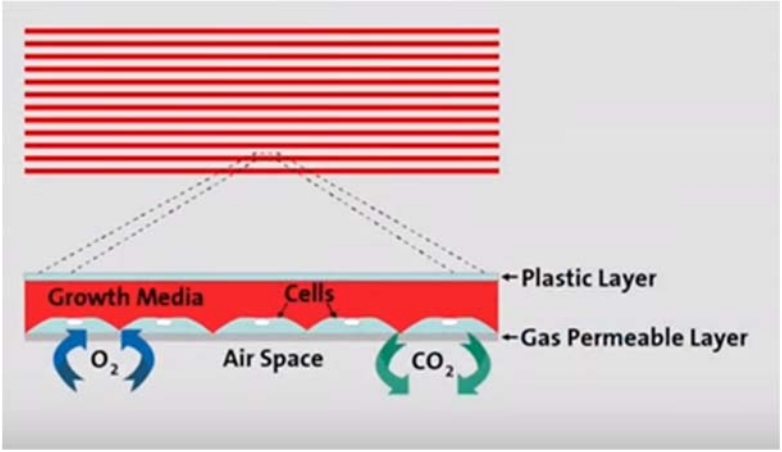
28. Brammer Bio has infringed at least claim 1 of the '192 Patent through its use of the HYPERStack, as set forth in the table below. The left side of the table contains the language of claim 1 of the '192 Patent. The right side of the table contains information on the HYPERStack and its use, including quoted text from an article entitled "Closed System Cell Culture Protocol Using HYPERStack Vessels with Gas Permeable Material Technology," authored by six Corning

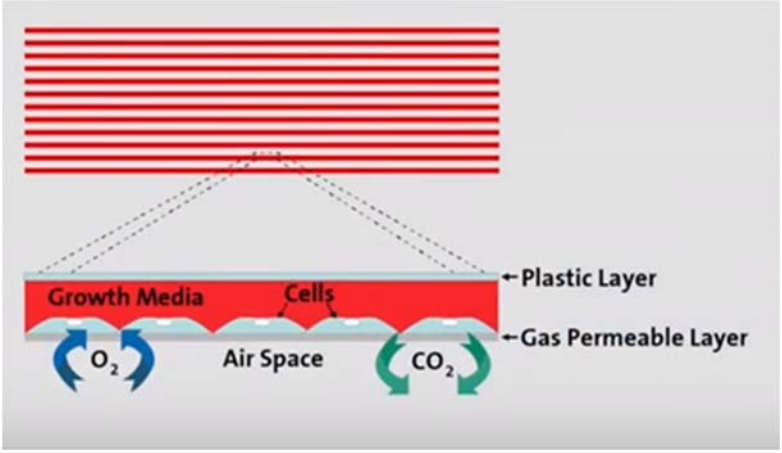
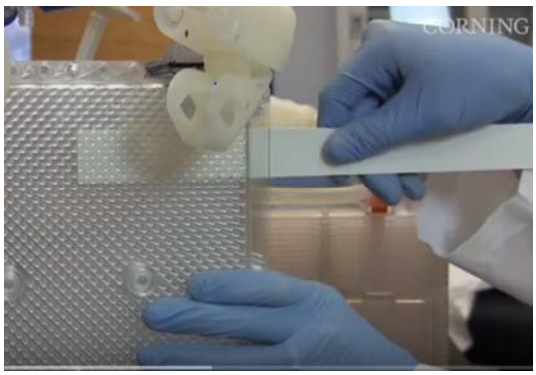
staff members, attached as Exhibit G, and images from Corning video entitled "Filling and Emptying the Corning® HYPERStack® Cell Culture Vessel," posted on YouTube at https://www.youtube.com/watch?v=6CPcW_qWu_w.

A method of culturing cells comprising:	The HYPERStack is used to culture cells. "The HYPERStack Vessel is a multilayered vessel for . . . culturing of cells. . . ." Exhibit G (Protocol ¶ 1(1)).
adding medium and animal cells into a static cell culture device	In use, medium and animal cells are added to the HYPERStack. The HYPERStack is a static cell culture device. "Inoculating Media": "Inject the Cell Suspension into the Media Bag and Mix well." "Using the bag stand, raise the media bag to help the cell suspension flow into the vessel." Exhibit G (Protocol ¶¶ 5(2), 6(5)).
that is not compartmentalized by a semi-permeable membrane,	The HYPERStack does not have a semi-permeable membrane.
at least a portion of said cell culture device is comprised at least in part of a nonporous gas permeable material,	"The HYPERStack vessels function via gas permeable material which allows gas exchange to occur. . . ." Exhibit G (Abstract ¶ 1).
ambient gas is in contact with at least a portion of said gas permeable material, and	"Rather than containing this 'headspace' for gas exchange within the vessel, the gas permeable products have air spaces . . . beneath each culture chamber which is open to the atmosphere." Exhibit G (Protocol ¶ 1(2)).
placing said cell culture device in a cell culture location that includes ambient gas at a composition suitable for animal cell culture,	"Move the HYPERStack vessel to the incubator." Exhibit G (Protocol ¶ 7(6)). Incubators used in cell culture contain ambient gas at a composition suitable for cell culture.

wherein said cell culture device is oriented in a position such that at least a portion of said cells reside upon at least a portion of said gas permeable material,	The HYPERStack is placed in the incubator such that at least some of the cells reside on the gas permeable material.  
the uppermost location of said medium is elevated beyond 2.0 cm from the lowermost location of said medium,	The uppermost location of medium is elevated more than 2.0 cm from the lowermost location of said medium, as can be seen in the picture above, from which the dimensions of the device filled with medium can be appreciated.
and said device is in a state of static cell culture.	The HYPERStack is cultured in a static state.

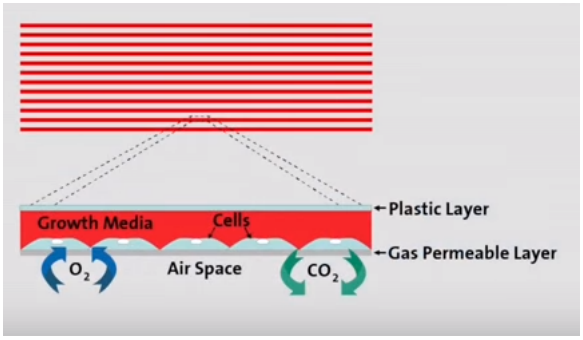
29. Brammer Bio has infringed at least claim 6 of the '317 Patent through its use of the HYPERStack, as set forth in the table below. The left side of the table contains the language of claim 6 of the '317 Patent. The right side of the table contains information on the HYPERStack and its use, including information authored by Corning staff, attached as Exhibit G.

A static cell growth apparatus comprising:	The HYPERStack is a static cell growth apparatus.
a liquid impermeable housing, the inside of which is able to contain cells and medium and the outside of which is in contact with ambient gas; and	The HYPERStack has a liquid impermeable housing which is able to contain cells and liquid medium. See Exhibit G (Protocol ¶ 7(6)) ("Fill the vessel until all of the inoculated media enters the vessel."). The outside of the housing in contact with ambient gas. See Exhibit G (Protocol ¶¶ 1(1), 1(2)) ("The HYPERStack vessel . . . relies on gas exchange through a . . . gas permeable polymer film. . . .") ("[T]he gas permeable products have air spaces . . . beneath each culture chamber which is open to the atmosphere.").
the housing defining a plurality of gas permeable shelves, each having an inside surface and an outside surface; and the inside surface of each shelf having an opposing surface located a distance away and defining a culture space; and	The HYPERStack housing defines multiple gas permeable shelves with an inside and outside surface, as shown below.  The inside surface of the gas permeable shelf has an opposing surface, called the "plastic layer" in the image above, with a culture space in between. There is a space below the outer surface of each gas permeable shelf, to allow gas contact. See Exhibit G (Protocol ¶ 1(2)) ("[T]he gas permeable products have air spaces . . . beneath each culture chamber which is open to the atmosphere.").

the culture spaces are located one above the other when the shelves are in a horizontal position; and	The culture spaces are located one above the other when the shelves are located in a horizontal position, as shown in the diagram below. 
a manifold that connects the culture spaces; and	A manifold connects the culture spaces. See Exhibit G (Protocol ¶ 2(2)) ("the Liquid Manifold connects each of the 12 stackette layers together within a HYPERStack module. * * * The manifold allows the user to make one fluid manipulation to the entire vessel.").
projections that make contact with the outside surface of each shelf while leaving a portion of the outside surface in contact with ambient gas.	Projections make contact with the outside surface of each shelf while leaving a portion of the outside surface in contact with ambient gas. The projections can be seen in the image below, in which paper is used to demonstrate the gas space. 

30. Brammer Bio has infringed at least claim 1 of the '443 Patent through its use of the HYPERStack, as set forth in the table below. The left side of the table contains the language of

claim 1 of the '443 Patent. The right side of the table contains information on the HYPERStack and its use, including information authored by Corning staff, attached as Exhibit G.

A method of culturing cells in a cell culture device comprised at least in part of a gas permeable material	The HYPERStack is a cell culture device comprised at least in part of gas permeable material. See Exhibit G (Protocol ¶ 2(1)) ("The Stackette is the individual cell culture compartment that is made up of the top plate and gas permeable film.").
and including at least one access port and including at least two scaffolds, the method comprising:	The HYPERStack has at least one access port. See Exhibit G (Protocol ¶ 2(5)) ("The Liquid handling tubing is connected to the liquid manifold and is used to make all closed system fluid manipulations."). The HYPERStack has at least two scaffolds. See Exhibit G (Protocol ¶¶ 2(1), 2(2)). ("The Stackette is the individual cell culture compartment that is made up of the top plate and gas permeable film. The cells are cultured within this compartment.") ("The Liquid Manifold connects each of the 12 stackette layers together within a HYPERStack module.").
a) adding cells and a volume of liquid medium into said cell culture device;	Cells and media are added into the HYPERStack. See Exhibit G (Protocol ¶ 6(6)) ("Using the bag stand, raise the media bag to help the cell suspension flow into the vessel.").
b) orienting said cell culture device into an inoculation position such that said scaffolds reside at different elevations within said cell culture device;	The device is oriented into a position such that the scaffolds reside one above the other at different elevations in the device as shown below. 

c) allowing cells to settle upon said scaffolds;	Cells settle upon the scaffolds, as shown in the diagram above.
d) adding enough liquid medium to prevent a unique gas-liquid interface from forming directly above at least one scaffold when the device is oriented in the inoculation position and to have at least a portion of the liquid medium in contact with at least a portion of said gas permeable material;	The user adds enough liquid medium to the HYPERStack to prevent a unique gas-liquid interface from forming above at least one scaffold when the device is in the inoculation position. See Exhibit F (Abstract ¶ 1) ("The HYPERStack vessels function via gas permeable material which allows gas exchange to occur, therefore eliminating the need for internal headspace within a vessel. The elimination of headspace allows the compartment where cell growth occurs to be minimized to reduce space, allowing more layers of cell growth surface area with the same volumetric footprint.") This can also be seen in the image below. 
e) placing the cell culture device in a cell culture location that includes ambient gas at a composition suitable for cell culture, said ambient gas making contact with said gas permeable material; and	The HYPERStack is placed in an incubator as shown in the image above. Incubators contain ambient gas at a composition suitable for cell culture. The HYPERStack has "air spaces . . . beneath each culture chamber which is open to the atmosphere." See Exhibit G (Protocol ¶ 1(2)).
f) not perfusing said liquid medium when said device is in said cell culture location.	The liquid medium in the HYPERStack is not perfused when the device is in the incubator.

COUNT I

INFRINGEMENT OF THE '192 PATENT, THE '317 PATENT AND THE '443 PATENT

31. Wilson Wolf incorporates by reference the above paragraphs as if stated herein.

32. The '192 Patent, the '317 Patent, and the '443 Patent (collectively "the Patents-in-Suit") are valid and enforceable.

33. Brammer Bio has directly infringed at least one claim of the '192 Patent, including, without limitation, Claim 1 of the '192 Patent to the harm and detriment of Wilson Wolf, and to the benefit and profit of Brammer Bio.

34. Brammer Bio has directly infringed at least one claim of the '317 Patent, including, without limitation, Claim 6 of the '317 Patent to the harm and detriment of Wilson Wolf, and to the benefit and profit of Brammer Bio.

35. Brammer Bio has directly infringed at least one claim of the '443 Patent, including, without limitation, Claim 1 of the '443 Patent to the harm and detriment of Wilson Wolf, and to the benefit and profit of Brammer Bio.

36. Brammer Bio's acts of direct infringement include, but are not limited to, its use of the HYPERStack cell culture vessel in the United States.

37. Brammer Bio's infringement is irreparably harming Wilson Wolf.

38. Wilson Wolf is entitled to money damages in an amount to be determined at trial, and to preliminary and permanent injunctive relief.

PRAYER FOR RELIEF

WHEREFORE, Wilson Wolf pray for relief as follows:

1. A judgment that Brammer Bio has infringed the '192 Patent, the '317 Patent, and the '443 Patent;

2. A judgment awarding Wilson Wolf damages in an amount to be determined at trial, but not less than a reasonable royalty;

3. An order enjoining Brammer Bio preliminarily, and permanently thereafter, from infringing, inducing infringement, and from contributing to the infringement of the '192 Patent, the '317 Patent, and the '443 Patent;

4. A judgment awarding Wilson Wolf its costs incurred herein, including attorneys' fees for an exceptional case pursuant to 35 U.S.C. § 285; and

5. A judgment awarding Wilson Wolf such other and further relief as the Court may deem just and equitable.

JURY DEMAND

Pursuant to Rule 38 of the Federal Rules of Civil Procedure, Wilson Wolf hereby demands a jury trial as to all issues so triable.

Dated: December 20, 2019

Respectfully submitted,

/s/ Kenneth L. Dorsney

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